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HUMAN PLACENTA-DERIVED STEM CELL S (HPDSC) AUGMENT TRANSPLANTATION WITH UMBILICAL CORD BLOOD

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This is the first report of a patient treated in a single-arm, non-randomized pilot study to assess the safety of human placenta-derived stem cells (HPDSC) transplantation with partially- or fully- HLA matched, related-donor umbilical cord blood (UCB) for malignant or non-malignant disorders requiring stem cell transplantation. HPDSC is being developed by Celgene Cellular Therapeutics (CCT) to augment the UCB stem cell graft. HPDSC is obtained by CCT's proprietary process involving perfusion of placental vasculature and is processed to remove red blood cells, non-viable cells and tissue debris. HPDSC is enriched in CD34+ cells and other progenitor cell types. Non-clinical studies have shown that augmenting a UCB transplant with HPDSC results in a higher likelihood of successful engraftment and an earlier engraftment as compared to UCB alone or HPDSC alone. It is hypothesized that the infusion of HPDSC following UCB transplantation will improve transplant outcome, shorten the time to neutrophil and/or platelet engraftment and diminish serious complications of the transplant procedure. The first patient is a 5 year old, 24 kg male with very high risk ALL in first remission. The subject underwent standard full ablative conditioning. GVHD prophylaxis consisted of steroids and cyclosporine. The subject was transplanted with a UCB unit (596.20×10^6 TNC, 73% post-thaw viability, 0.26% CD34+) and HPDSC unit (294×10^6 TNC, 63% post thaw viability, 0.85% CD34+) obtained from his HLA-matched sibling and processed/stored by LifeBankUSA, a wholly owned subsidiary of Celgene Corp. There were no clinically significant infusion reactions, and to date there have been no HPDSC-related serious adverse events. Myeloid engraftment occurred by Day +17 and platelet engraftment by Day+70. There was no evidence of serious infection nor aGVHD. Complete donor chimerism was evident by Day+30. The subject was discharged from the hospital on day +15. Subject is disease-free for more than 6 months post-transplant and his immune system is recovering as expected. Based upon this initial experience, infusion of HPDSC was safe and may have therapeutic benefit in augmenting cord blood transplantation. Continuation of the study is warranted.

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A HIGH INCIDENCE OF ACUTE GRAFT-VERSUS-HOST DISEASE IN UNRELATED CORD BLOOD TRANSPLANTATION IN PAEDIATRIC PATIENTS – A SINGLE CENTRE EXPERIENCE

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Introduction: Haematopoietic stem cell transplantation (HSCT) is the treatment of choice for certain malignant and inherited disorders in paediatric patients. The use of unrelated cord blood (UCB) as a stem cell source presents advantages which include immediate availability, less stringent HLA matching and less graft-versus-host disease (GVHD). Grade II to IV aGVHD has been reported to be between 14 to 36% in HLA 2/6 mismatched UCBT. We report a much higher incidence of aGVHD.

Materials: From 1997 till 2008, single UCB units from various international cord blood banks were imported for 31 patients. Indications for transplantation included ALL in 9 pts, AML 4, JMML 3, CML in CP 1, SAA 1, Thalassaemia 8 , Wiskott-Aldrich syndrome 2 and Osteopetrosis 3. Cord blood units were 3,4, 5 or 6 HLA matched units for 1, 18, 9 and 3 recipients consecutively. Conditioning regimen for ALL included TBI and CY ± ATG ±Thiotepa. Patients with AML received BU and CY±ATG while the majority of non-malignant disorders were conditioned with BU+CY+ATG. Prophylaxis against GVHD used cyclosporine(CSA) with low dose MTX or prednisolone or CSA alone. Treatment of GVHD included methyprednisolone, ATG, MMF and infliximab.

Results: The median age was 5 years (range 0.7–13 years) and weight was 17.5 kg (5.56–50.2 kg). Median nucleated cell dose was 8.7×10^7/kg (range 2.6–29.3) while median CD34+ cell dose was 2.6×10^5/kg (range 0.48–12.2). Four patients were early deaths and not evaluable for engraftment. Twenty out of 27 pts (74%) experienced neutrophil engraftment at a median of D25 (range 12–36) and platelet >20K at a median of D46 (36–183) while primary graft failure occurred in 7 pts (26%). AGVHD occurred in 19/20 pts with clinical grades I, II, III and IV occurring in 1,7,7 and 4 pts respectively. Of the 11 pts with grades III and IV aGVHD (55%), 3 were alive while 8 succumbed to infection or multiorgan failure. Chronic GVHD occurred in 3/13 evaluable pts where 1 was extensive. VOD occurred in 9 pts. Mortality occurred in 17/31 pts (55%). Survival was seen in 14 pts (45%) with follow up from 5–95 months.

Conclusion: We experienced a 95% incidence of aGVHD and more than half of them were severe clinical grade III and IV which directly contributed to mortality of patients.

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OUTCOMES OF HEMATOPOIETIC STEM CELL TRANSPLANTATION (HCT) FROM UMBILICAL CORD BLOOD (UCB) UNITS IN PATIENTS WITH MALIGNANT AND NON-MALIGNANT DISORDERS

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HCT is a curative treatment option for high risk malignant and non-malignant diseases. HLA-identical donors are the preferred graft sources. Matched unrelated donors have been utilized successfully for the last two decades. However, in about 30% of all patients neither an HLA-matched sibling nor a MUD donor is available; for these patients UCB has become an acceptable stem cell source. UCB offers several advantages: rapid availability, the possibility of using HLA-mismatched units and a decreased risk of GVHD. We analyzed the treatment outcomes in patients who have undergone HCT using UCB at City of Hope. 45 patients with malignant (82%) and non-malignant (18%) hematological disorders received 46 HCT using allogeneic or autologous UCB from January 1, 1997 through June 31, 2007. 29 patients (66%) carried a diagnosis of acute leukemia. 36 patients received single cord unit (including 2 autologous transplants), 10 patients received two UCB units. 80% of patients were alive at day 100. 1 year and estimated 5-year overall survival (0S) was 53% (95% CI 38%–89%) and 43% (95% CI 28%–64%) respectively with median follow up of patients alive at date of analysis of 4.2 years. Estimated 5-year survival for single (excluding autologous), double and autologous UCB transplant was 44% (95% CI 27%–60%), 28% (95% CI 4%–59%) and 100% respectively. Degree of HLA mismatch impacted OS – patients receiving UCB mismatched at 0 or 1 loci had significantly better 5-year survival (61%, 95% CI 40%–77%) compared to patients transplanted with 2 to 3 antigen mismatched units (17% 95% CI 4%–36%) $p = 0.005$. Neutrophil engraftment occurred at median 26 days (89% of patients engrafted by day 53). The incidence and time to platelet engraftment to 20K and 50K was 76% (median 50.5 days) and 67% (median 69 days) respectively. 62% of patients receiving single UCB developed acute GVHD (44% grade 1–2; 18% grade 3–4). 23% of these patients developed chronic GVHD (20% limited, 3% severe). All patients who received two UCB units developed acute GVHD (80% grade 1–2, 20% grade 3–4; and later chronic GVHD). 14 patients (30%) developed CMV infection (4 prior to day 30, 7 within days 30–100, 3 post day 100). 26% of patients had culture proven viral infections. In conclusion, for patients with high risk disease lacking HLA-matched sibling donor, UCB can offer a rapidly available alternative source of stem cells with transplant outcomes comparable to the results achieved using matched unrelated donors.

LATE EFFECTS/QUALITY OF LIFE

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DIABETES MELLITUS (DM) AND HYPERTENSION (HTN) IN ADULT AND PEDIATRIC SURVIVORS OF ALLOGENEIC HEMATOPOIETIC-CELL TRANSPLANTATION (HCT)

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DM and HTN are frequent early complications of allogeneic HCT; however, their long-term outcome is not well known. We